

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service on the date shown below with sufficient postage as First Class Mail, in an envelope addressed to: MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: January 4, 2007

Signature:

Shelley Danek
(Shelley C. Danek, Ph.D.)

Docket No.: 28646/42267
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re Patent Application of:
Roger Melton et al.

Application No.: 10/590,789

Confirmation No.: N/A

Filed: August 25, 2006

Art Unit: 0

For: Use of Carboxypeptidase G for Combating
Antifolate Toxicity

Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 CFR 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 CFR 1.97(b)(3)).

In accordance with 37 CFR 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents and U.S. patent applications. Applicant submits herewith copies of foreign patents and non-patent literature in accordance with 37 CFR 1.98(a)(2).

In accordance with 37 CFR 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR 1.56(a) exists. In accordance with 37 CFR

1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

It is submitted that the Information Disclosure Statement is in compliance with 37 CFR 1.98 and the Examiner is respectfully requested to consider the listed references.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 13-2855, under Order No. 28646/42267. A copy of this paper is enclosed.

Dated: January 4, 2007

Respectfully submitted,

By Shelley Danek

Shelley C. Danek, Ph.D.

Registration No.: 57,712

MARSHALL, GERSTEIN & BORUN LLP

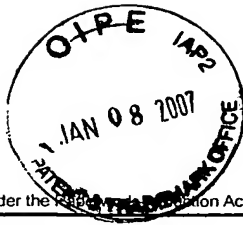
233 S. Wacker Drive, Suite 6300

Sears Tower

Chicago, Illinois 60606-6357

(312) 474-6300

Agent for Applicant



PTO/SB/08A/B (09-06)

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Application Number	10/590,789
				Filing Date	August 25, 2006
				First Named Inventor	Roger Melton
				Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
Sheet	1	of	3	Attorney Docket Number	28646/42267

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		US-20040014187-A1	01-22-2004	Springer et al.	

FOREIGN PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		EP 0 12 352	10-10-1984	Atkinson et al.	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. * CITE NO.: Those application(s) which are marked with an single asterisk (*) next to the Cite No. are not supplied (under 37 CFR 1.98(a)(2)(iii)) because that application was filed after June 30, 2003 or is available in the IFW. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Abelson et al., "High-Dose Methotrexate-Carboxypeptidase G ₁ -A Selective Approach to the Therapy of Central Nervous System Tumors", <i>Developments in Biochemistry</i> , 4:629-634 (1979)	
		Adamson et al., "Rescue of Experimental Intrathecal Methotrexate Overdose with Carboxypeptidase-G ₂ ", <i>J. Clin. Oncol.</i> , 9:670-674 (1991).	
		Adamson et al., "Methotrexate Pharmacokinetics Following Administration of Recombinant Carboxypeptidase-G ₂ in Rhesus Monkeys", <i>Journal of Clinical Oncology</i> , 10:1359-1364 (1992)	
		Bleyer, "The Clinical Pharmacology of Methotrexate. New Applications for an Old Drug," <i>Cancer</i> , 41:36-51 (1978).	
		Bloom et al., "The antifolate AG2037 utilizes hypoxanthine salvage as an important rescue mechanism", <i>Proc Amer Asso Cancer Res Annu Meet</i> , 43:59	
		Castro, "Thymidine rescue: an antidote for pemetrexed-related toxicity in the setting of acute renal failure", <i>J. Clin. Oncol.</i> , 21:4066 (2003)	
		Chabner et al., "Enzymatic Cleavage of Methotrexate Provides a Method for Prevention of Drug Toxicity," <i>Nature</i> , 239:395-397 (1972)	
		Chambers et al., "Plasmid pMTL153: a high copy number version of pAT153 and its use to obtain high expression of the Pseudomonas carboxypeptidase G ₂ gene", <i>Appl. Microbiol. Biotechnol.</i> , 29:572-578 (1998)	
		Clarke et al., "Clinical and Preclinical Pharmacokinetics of Raltitrexed," <i>Clin. Pharmacokinet</i> , 39(6):429-443 (2000)	
		Condit et al., "Renal Toxicity of Methotrexate," <i>Cancer</i> , 23:126-131 (1969)	
		DeAngelis et al., "Carboxypeptidase G ₂ Rescue After High-Dose Methotrexate", <i>Journal of Clinical Oncology</i> , 14:2145-2149 (1996)	
		Dowell et al., "New Mustard Prodrugs for Antibody-Directed Enzyme Prodrug Therapy: Alternatives to the Amide Link," <i>J. Med. Chem.</i> , 39:1100-1105 (1996)	
		Dreicer et al., "A Phase II Trial of Edatrexate in Patients with Advanced Renal Cell Carcinoma", <i>Am. J. Clin. Oncol.</i> , 20(3):251-253 (1997)	
Examiner Signature		Date Considered	

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	10/590,789
				Filing Date	August 25, 2006
				First Named Inventor	Roger Melton
				Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
Sheet	2	of	3	Attorney Docket Number	28646/42267

		Farrugia et al., "Leucovorin Rescue from Raltitrexed (Tomudex)-induced Antiproliferative Effects: <i>In Vitro</i> Cell Line and <i>In Vivo</i> Mouse Studies", <i>Clinical Cancer Research</i> , 6:3646-3656 (2000)	
		FDA grants orphan drug designation for voraxaze, Protherics PLC (2003)	
		Franchi et al., "Favorable Toxicity Profile of Raltitrexed in Elderly Patients Treated for Colorectal Cancer: A Case Series," <i>Gerontology</i> , 49(5):324-327 (2003)	
		Goldman, "Membrane Transport of Methotrexate (NSC-740) and Other Folate Compounds: Relevance to Rescue Protocols," <i>Cancer Chemo Rep.</i> , 6:63-72 (1975)	
		Jackman et al., "ICI D1694, a Quinazoline Antifolate Thymidylate Synthase Inhibitor That is a Potent Inhibitor of L1210 Tumor Cell Growth <i>In Vitro</i> and <i>In Vivo</i> : A New Agent for Clinical Study", <i>Cancer Research</i> , 51:5579-5586 (1991)	
		Johansen et al., "Final results of a phase I and pharmacokinetic study of γ -methylene-10-deazaaminopterin (MDAM) administered intravenously daily for five consecutive days in patients with solid tumors", <i>Cancer Chemother. Pharmacol.</i> , 53:370-376 (2004)	
		Jolivet et al., "The Pharmacology and Clinical Use of Methotrexate," <i>N. Engl. J. Med.</i> , 309:1094-1104 (1983)	
		Kalghatgi et al., "Folate-Degrading Enzymes: A Review with Special Emphasis on Carboxypeptidase G," <i>In: Enzymes as Drugs</i> , J Holcenberg and J Roberts, eds, Wiley, New York, pp.77-102 (1981).	
		Kintzel, "Anticancer Drug-Induced Kidney Disorders," <i>Drug Safety</i> , 24:19-38 (2001)	
		Kisliuk, "Deaza Analogs of Folic Acid as Antitumor Agents," <i>Current Pharmaceutical Design</i> , 9(31):2615-2625 (2003).	
		Krackhardt et al., "Carboxypeptidase G ₂ Rescue in a 79 Year-Old Patient With Cranial Lymphoma After High-Dose Methotrexate Induced Acute Renal Failure", <i>Leuk. Lymph.</i> , 35:631-635 (1999)	
		Krause et al., "Carboxypeptidase-G ₂ Rescue in Cancer Patients with Delayed Methotrexate Elimination after High-dose Methotrexate Therapy", <i>Leukemia and Lymphoma</i> , 43(11):2139-2143 (2002)	
		Krug et al., "Phase I and Pharmacokinetic Study of 10-Propargyl-10-deazaaminopterin, a New Antifolate ¹ ", <i>Clinical Cancer Research</i> , 6:3493-3498 (2000)	
		Kuriakose et al., "Phase I Trial of Edatrexate in Advanced Breast and Other Cancers", <i>Cancer Investigation</i> , 20(4):473-479 (2002)	
		Mantadakis et al., "Delayed Methotrexate Clearance in a Patient With Sickle Cell Anemia and Osteosarcoma", <i>J. Pediat. Hematol. Oncol.</i> , 21:165-169 (1999)	
		Massacesi et al., "Raltitrexed-Induced Hepatotoxicity: Multivariate Analysis of Predictive Factors," <i>Anticancer Drugs</i> , 14(7):533-541 (2003).	
		McCullough et al., "Purification and Properties of Carboxypeptidase G ₁ ," <i>J. Biol. Chem.</i> , 246:7207-7213 (1971).	
		McGuire, "Anticancer Antifolates: Current Status and Future Directions," <i>Current Pharmaceutical Design</i> , 9(31):2593-2613 (2003)	
		Meyers et al., "Phase II trial of edatrexate in relapsed or refractory germ cell tumors: A Southwest Oncology Group Study (SWOG 9124)", <i>Investigational New Drugs</i> , 16:347-351 (1999)	
		Minton et al., "Molecular Cloning of the <i>Pseudomonas</i> Carboxypeptidase G ₂ Gene and its Expression in <i>Escherichia coli</i> and <i>Pseudomonasputida</i> ," <i>J. Bacteriol.</i> , 156:1222-1227 (1983)	
		Minton et al., "The Complete Nucleotide Sequence of the <i>Pseudomonas</i> Gene Coding for Carboxypeptidase G ₂ ," <i>Gene</i> , 31(1-3):31-38 (1984)	
		Minton et al., "Identification of the Promoter of the <i>Pseudomonas</i> Gene Coding for	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)				Complete if Known	
				Application Number	10/590,789
				Filing Date	August 25, 2006
				First Named Inventor	Roger Melton
				Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
Sheet	3	of	3	Attorney Docket Number	28646/42267

	Carboxypeptidase G2," <i>J. Mol. Appl. Genet.</i> , 3(1):26-35 (1985)	
	Mohty et al., "Carboxypeptidase G2 Rescue in Delayed Methotrexate Elimination in Renal Failure," <i>Leuk. Lymphoma</i> , 37:441-443 (2000)	
	Nguyen et al., "Pharmacokinetics studies and toxicity profile of raltitrexed used by intraperitoneal route in normothermia in a pig model", <i>Med. Sci. Monit.</i> , 9(1):BR37-42 (2003)	
	O'Marcaigh et al., "Successful Treatment of Intrathecal Methotrexate Overdose by Using Ventriculolumbar Perfusion and Intrathecal Instillation of Carboxypeptidase G ₂ ", <i>Mayo Clin. Proc.</i> , 71:161-165 (1996)	
	Patterson et al., "Thymidine Phosphorylase Moderates Thymidine-dependent Rescue after Exposure to the Thymidylate Synthase Inhibitor ZD1694 (Tomudex) <i>In Vitro</i> ", <i>Cancer Research</i> , 58:2737-2740 (1998)	
	Pinedo et al., "The Reversal of Methotrexate Cytotoxicity to Mouse Bone Marrow Cells by Leucovorin and Nucleosides," <i>Cancer Res.</i> , 36:4418-4424 (1976).	
	Pisters et al., "High-Dose Edatrexate with Oral Leucovorin Rescue: A Phase I and Clinical Pharmacological Study in Adults with Advanced Cancer", <i>Clinical Cancer Research</i> , 2:1819-1824 (1996)	
	Purcell et al., "Novel Antifolate Drugs," <i>Current Oncology Reports</i> , 5(2):114-125 (2003).	
	Rowell et al., "Crystal Structure of Carboxypeptidase G ₂ , a Bacterial Enzyme with Applications in Cancer Therapy," <i>Structure</i> , 5(3):337-347 (1997).	
	Sherwood et al., "Purification and Properties of Carboxypeptidase G ₂ from <i>Pseudomonas sp.</i> Strain RS-16. Use of a Novel Triazine Dye Affinity Method," <i>Eur. J. Biochem.</i> , 148:447-453 (1985)	
	Springer et al., "Optimization of Alkylating Agent Prodrugs Derived from Phenol and Aniline Mustards: A New Clinical Candidate Prodrug (ZD2767) from Antibody-Directed Enzyme Prodrug Therapy," <i>J. Med. Chem.</i> , 38:5051-5065 (1995).	
	Summary of Product Characteristics: Voraxaze™ (Carboxypeptidase G2) Enact Pharma plc, 2003.	
	Thödtmann et al., "A phase II trial of pemetrexed in patients with metastatic renal cancer", <i>Investigational New Drugs</i> , 21:353-358 (2003)	
	Thompson et al., "Improving the Sensitivity of Progressive Multiple Sequence Alignment through Sequence Weighting, Position-Specific Gap Penalties and Weight Matrix Choice," <i>Nucleic Acids Res.</i> , 22:4673-4680 (1994).	
	"Tomudex" Patient Information Leaflet P003746, Astra Zeneca (2001)	
	Tsavaris et al., "Raltitrexed (Tomudex) Administration in Patients with Relapsed Metastatic Colorectal Cancer After Weekly Irinotecan/5-Fluorouracil/Leucovorin Chemotherapy," <i>BMC Cancer</i> , 2(1):2 (2002).	
	Von Poblozki et al., "Carboxypeptidase-G2 Rescue in a Woman with Methotrexate-Induced Renal Failure," <i>Med. Klin.</i> , 95:457-460 (2000).	
	Widemann et al., "Carboxypeptidase-G ₂ , Thymidine, and Leucovorin Rescue in Cancer Patients with Methotrexate-Induced Renal Dysfunction", <i>Journal of Clinical Oncology</i> , 15:2125-2134 (1997)	
	Widemann et al., "Rescue with Carboxypeptidase-G ₂ (CPDG ₂) and Leucovorin (LV) for Patients with High-Dose Methotrexate (HDMTX) Induced Renal Failure", <i>Proc Annu Meet Am Soc Clin Oncol.</i> , 17:A855 (1998)	
	Widemann et al., "Pharmacokinetics and Metabolism of the Methotrexate Metabolite 2,4-Diamino-N10-Methylpterioic Acid," <i>J. Pharmacol. Expel. Therapy</i> , 294:894-901 (2000).	
	Zoubek et al., "Successful Carboxypeptidase G2 Rescue in Delayed Methotrexate Elimination Due to Renal Failure", <i>Pediatric and Hematology and Oncology</i> , 12:471-477 (1995)	

Examiner Signature		Date Considered	
--------------------	--	-----------------	--